

## RESEARCH NOTE

### Outbreak of echovirus 13 infection among Lithuanian children

I. Narkeviciute and D. Vaiciuniene

Vilnius University, Centre of Pediatrics, Vilnius, Lithuania

#### ABSTRACT

The aim of this study was to investigate an outbreak of enterovirus infection in Lithuania in 2001, as well as the clinical presentation and outcome of the disease. Thirty children aged 1 month to 15 years were referred to hospital with suspected enterovirus infection during the period August–October 2001. Echovirus 13 (EV-13) was isolated from eight (26.7%) cases. No other pathogens were detected. Infection presented predominantly as viral meningitis, and rarely as a febrile illness with rash. The outcome was good for all patients. This is the first report of EV-13 from Lithuania.

**Keywords** Children, echovirus, EV-13, Lithuania, meningitis, viral meningitis

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Enteroviruses, including echoviruses, are the commonest cause of viral meningitis and also cause other human diseases (e.g., non-specific rashes, fever, diarrhoea, respiratory disease and encephalitis) [1,2]. Before 2000, echovirus type 13 (EV-13) was isolated only rarely worldwide. In Germany, EV-13 was not isolated between 1996 and 1999, but became the predominant serotype in 2000. Also in 2000, isolation of EV-13 was notified from France [3], Spain [4] and Israel [5], and in 2001 from the USA [6,7] and Japan [8].

In 2001, the morbidity from enteroviral infections, including viral meningitis, increased in the Vilnius region of Lithuania. In total, 154 patients with clinical enterovirus infection were treated at the Vilnius University Children's Hospital, including 117 (76%) treated during the July–October epidemic period, which peaked in August. These comprised 75 children treated for enterovirus infection (code B34.1 of the 10th International Disease Classification [9]) and 42 children treated for viral meningitis (code A87.9). Between 13 August and 18 October 2001, 30 children diagnosed in the emergency room with suspected enterovirus infection were examined and treated at the Centre of Paediatrics. In addition to the usual general clinical examination and biochemical and microbiological laboratory tests, samples were transported frozen to the Lithuanian National Virological Laboratory, and the presence of enteroviruses in faecal specimens, throat swabs and cerebrospinal fluid (CSF) was investigated by conventional cell culture methods following World Health Organization (WHO) recommendations [10]. Cultures that exhibited a characteristic cytopathic effect for enteroviruses were identified by the standard method of microneutralisation [10].

Fifty-five faecal specimens from 30 children (two specimens taken from 25 children at 1–2-day intervals, and five single specimens), throat swabs from 20 children and CSF specimens from 13 children were tested. A case of enterovirus meningitis was defined as the presence of enterovirus in CSF or stool, and increased lymphocyte counts in CSF, combined with an absence of bacterial growth on culture.

Of the 30 children (23 males) with suspected enterovirus infection, 13 had viral meningitis, 11 gastroenteritis or gastritis, three a respiratory tract infection, and three a febrile illness with non-specific skin rash. The children were hospitalised for a median of 2.9 days (range 1–9 days); EV-13 was isolated from the faeces of eight (26.7%) children (twice for one child), and the throat swabs were also positive for one child. The echovirus was not found in CSF. All EV-13-positive specimens were obtained between days 1 and 3 after admission. The age of the EV-13-positive patients ranged from 1.5 months to 14 years (median 7.5 years); two patients were aged < 6 months (1.5 and 5 months, respectively).

Corresponding author and reprint requests: I. Narkeviciute, Vilnius University, Centre of Paediatrics, Santariskiu 4, 2021 Vilnius, Lithuania  
E-mail: irena.narkeviciute@ivuvl.vu.lt

**Table 1.** Clinical symptoms and signs of patients with suspected enterovirus infection

Clinical data	All patients <i>n</i> = 30	EV-13 viral culture	
		Positive <i>n</i> = 8	Negative <i>n</i> = 22
Highest temperature			
37.5–38°C	13	4	9
38.1–39°C	11	4	7
> 39.1°C	5	0	5
Duration of fever			
Range (days)	1–7	1–4	1–7
Mean (days)	3.1	2.3	3.1
Positive meningeal signs	14	6	8
Rash	6	2	4
Vomiting	20	4	16
Diarrhoea	11	1	10

All eight patients with laboratory-confirmed EV-13 infection had fever (Table 1), six of the older children had headache, and two infants showed irritability. The two infants with confirmed EV-13 infection had fever for 3 and 4 days, respectively, and skin rash. The blood leukocyte counts of the eight EV-13-positive patients ranged from 6.3 to  $15.5 \times 10^9$  cells/L (mean  $10.4 \times 10^9$  cells/L), while the C-reactive protein concentration was within the normal range. In the six patients with EV-13 meningitis, the median CSF leukocyte count was 131 cells/mm<sup>3</sup> (range 31–320 cells/mm<sup>3</sup>), with neutrophils predominant in three patients. The mean CSF protein value was 0.264 g/L (range 0.193–0.354 g/L) and the median CSF glucose concentration was 3.2 mmol/L (range 2.5–3.7 mmol/L). No bacterial growth was observed in any of the CSF cultures. Based on the clinical and laboratory assessments, it was concluded that six of the eight patients from whom EV-13 was isolated had meningitis, while two (both infants) had enterovirus infection with fever and a non-specific rash. Of the 22 patients who tested negative for enterovirus, seven (31.8%) were diagnosed as having a non-confirmed enterovirus infection (including two patients with viral meningitis). Of the other 15 patients, six had bacterial gastroenteritis, two had pneumonia, and seven had another disease such as pharyngitis, urinary tract infection, encephalitis or fever of unknown origin (seven patients). Following initial hospitalisation, three of the eight EV-13-positive children were treated in the intensive care unit, with a median hospital stay of 4.6 days. All children recovered.

Before 2001, the enterovirus isolated most frequently in Lithuania was EV-30, with other en-

teroviruses being isolated only rarely [11]. In 2000, outbreaks of EV-13 meningitis were reported in several European countries [2–4,12] and Israel [5], but as EV-13 has been isolated rarely, the spectrum of disease associated with this virus has not yet been well-established. Aseptic meningitis was the predominant illness associated with EV-13 activity in Europe in 2000 and in the USA in 2001 [2,12,13]. Other clinical diagnoses of EV-13 infection include febrile illness, diarrhoea and rash. Asymptomatic carriage occurs more rarely [2,7].

The present study demonstrated EV-13 meningitis in six children, and febrile illness with non-specific skin rash in two children. The laboratory findings were typical of viral meningitis, although half of the patients had >50% neutrophils in their CSF. Similar clinical and laboratory findings in cases of EV-13 meningitis have been reported previously [4–6,14]. Thus, the possible presence of enteroviruses should be investigated in meningitis patients and subjects showing non-specific rash and fever. The age distribution of patients from whom EV-13 was isolated was similar to that observed in the USA, Israel and Germany, where most EV-13-related meningitis patients were young children. However, older children were affected in England and Wales [12]. The final conclusion of the present study was that the 2001 enterovirus infection outbreak in Lithuania was caused by EV-13. This is the first time that EV-13 has been detected in Lithuania.

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## RESEARCH NOTE

### Molecular epidemiology of astrovirus infection in Italian children with gastroenteritis

S. De Grazia<sup>1</sup>, G. M. Giammanco<sup>1</sup>,  
C. Colomba<sup>2</sup>, A. Cascio<sup>3</sup> and S. Arista<sup>1</sup>

<sup>1</sup>Dipartimento di Igiene e Microbiologia, <sup>2</sup>Istituto di Patologia Infettiva e Virologia, Università di Palermo, Palermo and <sup>3</sup>Clinica delle Malattie Infettive, Università di Messina, Messina, Italy

### ABSTRACT

A 1-year study involving 157 gastroenteritis samples was conducted to investigate the role of human astrovirus (HAstV) as a cause of gastroenteritis in Italian children aged <2 years. The overall incidence of HAstV was 3.1%. Most cases

occurred between March and May, and four of the five isolates were of the HAstV-1 type, the other being HAstV-3. Analysis of genetic variability showed that the three HAstV-1 isolates collected in 2000 clustered together, but separately from the 1999 isolate. The results indicated that HAstV should be considered as a potential diarrhoeal pathogen in Italian children.

**Keywords** Astrovirus, children, diarrhoea, gastroenteritis, typing

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Human astroviruses (HAstVs) have been identified increasingly worldwide as agents of infantile gastroenteritis [1]. Associated initially with focal outbreaks of diarrhoea, they have also been implicated occasionally in nosocomial infections and with persistent gastroenteritis in immunocompromised hosts [2,3]. Their incidence in children with gastroenteritis in both developed and developing countries is usually 2–9% [1]. The astrovirus virion is composed of a non-enveloped capsid and a single-stranded (positive) RNA genome, which includes three open reading frames (ORFs). A 348-bp nucleotide sequence of ORF2, which codes for the capsid proteins, has been used to classify HAstVs into eight genotypes [4]. Previous studies in various countries have shown that HAstV-1 is the most common type causing disease, whereas types HAstV-6, -7 and -8 have been detected only rarely [4]. The aims of the present study were: (1) to define the epidemiological role of HAstV as a cause of gastroenteritis in Italian children; (2) to compare HAstV-related illnesses with those caused by other enteric viruses; and (3) to analyse the potential genetic correlation between any HAstV isolates obtained and prototype strains from other geographical areas.

The study was performed with 439 children aged <2 years who were admitted to the G. Di Cristina Children's Hospital (Palermo, Italy) with acute diarrhoea (at least three watery stools in 24 h, with a sudden onset) between August 1999 and July 2000. Medical staff interviewed the accompanying adults, examined the children, and recorded demographic data (sex and age)

Corresponding author and reprint requests: S. Arista, Dipartimento di Igiene e Microbiologia, Università di Palermo, Via del Vespro 133-90127, Palermo, Italy  
E-mail: arista@unipa.it